

Remarks

The Examiner is thanked for the Office Action mailed 10/03/2002 (request for 1-month extension to respond, enclosed) and the indication of allowability of claim 62 if rewritten to include all of the limitations of the base claim and any intervening claims. Accordingly, the limitations of claims 60, 61 and 62 have been added to claim 51. Note that the limitation of intervening claim 56 has also been added to claim 51 since claim 60 already referred to "nonionic surfactant" (a particular species of claim 56). Claims 60-62, 68 have been canceled and the remainder of the claims have been made directly or indirectly on claim 51 (which again now contains all the limitations of indicated allowable claim 62). Claim 56, 57 have been amended to delete the "nonionic" surfactant reference (which is now in claim 51). Accordingly, it is believed that claims 51-59, 63-68 are now in condition for allowance.

It is noted that while the Examiner combined references to try to establish obviousness, claim 51 always required the presence of "a surfactant of a type and present at a concentration effective to substantially reduce nonspecific binding and promote mixing of components within the sample fluid". Further, it was demonstrated that background interference was unexpectedly reduced with the presence of appropriate types and amounts of surfactants. See page 31 of the application describing examples (including the now claimed surfactant class) which reduced background interference, such as shown in FIG. 9 (with surfactant) versus FIG. 8 (without the appropriate type and amount of surfactant). The Examiner has not pointed to any such benefit disclosed or suggested by combining the prior art references in the manner suggested by the Examiner. However, in the interests of expediting prosecution of the present application all of the claims now include the limitations of claim 62 (and intervening claims) which was indicated as allowable.

The present amendment also adds new dependent claims 69-71 which additionally specify that the substrate has "a silane functionalized surface" (described, for example in the last paragraph beginning at the bottom of p. 15 of the present application). Accordingly new dependent claims 69-71 should also be in condition for allowance.

Accordingly, it is believed that claims 51-59, 63-71 are now in condition for allowance. If the Examiner is of the view that there are any outstanding issues, he is invited to call Gordon Stewart at (650)485-2386.

Respectfully submitted,



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APPENDIXShowing All Amendments Now Being Made

51. (AMENDED) A method for conducting a hybridization assay within an enclosed hybridization chamber, comprising:

(a) providing a device comprised of a (i) a substrate having a surface with at least a portion of said surface representing a hybridization region, wherein a plurality of oligonucleotide probes are bound to the substrate surface within the hybridization region and arranged in a spatially defined and physically addressable manner, and (ii) a cover which sealingly contacts the substrate surface about the hybridization region, wherein the cover and the hybridization region form an enclosure having an interior space comprising a hybridization chamber; and

(b) introducing into the hybridization chamber a sample fluid comprising (i) a target molecule which may hybridize to a surface-bound molecular probe within the hybridization region, (ii) a hybridization buffer, and (iii) a surfactant of a type and present at a concentration effective to substantially reduce nonspecific binding and promote mixing of components within the sample fluid; and

(c) maintaining hybridization conditions within the hybridization chamber for a period of time sufficient to allow hybridization between the target molecule and a surface-bound molecular probe to occur;

wherein the surfactant is a polymeric nonionic surfactant which is polyethylene oxide.

52. The method of claim 51, wherein the hybridization chamber has a volume in the range of about 0.2 μl to about 312 μl .

53. The method of claim 52, wherein the hybridization chamber has a volume in the range of about 1 μl to about 200 μl .

54. The method of claim 52, wherein the hybridization region has an area in the range of about 4 mm² to about 500 mm².

55. The method of claim 53, wherein the hybridization region has an area in the range of about 20 mm² to about 350 mm².

56. (AMENDED) The method of claim 51, wherein the surfactant additionally comprises a surfactant is-selected from the group consisting of anionic surfactants, cationic surfactants, amphoteric surfactants, ~~nonionic surfactants~~, and combinations thereof.

57. (AMENDED) The method of claim 56, wherein the additional surfactant is an anionic surfactant.

58. The method of claim 57, wherein the anionic surfactant is a sodium, potassium, ammonium or lithium salt of lauryl sulfate.

59. The method of claim 58, wherein the anionic surfactant is lithium lauryl sulfate.

~~60. The method of claim 56, wherein the surfactant is a nonionic surfactant.~~

~~61. The method of claim 60, wherein the nonionic surfactant is polymeric.~~

~~62. The method of claim 61, wherein the nonionic surfactant is polyethylene oxide.~~

63. The method of claim 51, wherein the surfactant represents in the range of approximately 0.1 wt.% to 10 wt.% of the sample fluid.

64. The method of claim 63, wherein the surfactant represents in the range of approximately 0.5 wt.% to 5 wt.% of the sample fluid.

65. The method of claim 64, wherein the surfactant represents in the range of approximately 0.75 wt.% to 5 wt.% of the sample fluid.

66. The method of claim 51, wherein the surfactant comprises a combination of polyethylene oxide and lithium lauryl sulfate, and further wherein the polyethylene oxide represents up to about 1 wt.% of the sample fluid and the lithium lauryl sulfate represents up to about 0.5 wt.% of the sample fluid.

67. The method of claim 51, wherein an air bubble is present within the hybridization chamber.

~~68. A method of mixing a fluid in an enclosed chamber having a height less than approximately 0.5 mm, comprising the steps of:~~

- ~~(a) providing a chamber having a height of less than about 0.5 mm;~~
- ~~(b) introducing into the chamber (i) a fluid containing molecular components, and (ii) an air bubble;~~
- ~~(c) sealing the chamber; and~~
- ~~(d) moving the chamber so as to create movement of the bubble within the fluid,~~

~~whereby mixing of the molecular components within the fluid is effected by displacement of the fluid as the bubble moves within the chamber.~~

69. (NEW) A method according to claim 51 wherein the surface is a silane functionalized surface.

70. (NEW) A method according to claim 56 wherein the surface is a silane functionalized surface.

71. (NEW) A method according to claim 58 wherein the surface is a silane functionalized surface.